Dated: May 16, 2000.

Margaret H. McFarland,

Deputy Secretary.

[FR Doc. 00–12756 Filed 5–25–00; 8:45 am]

BILLING CODE 8010–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 176

[Docket No. 00F–0813]

Indirect Food Additives: Paper and Paperboard Components

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of sodium xylenesulfonate as a component of paper and paperboard intended to contact food. This action is in response to a petition filed by Tritex Co., Inc.

DATES: This rule is effective May 26, 2000. Submit written objections and requests for a hearing by June 26, 2000.

ADDRESSES: Submit written objections to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Mark A. Hepp, Center for Food Safety and Applied Nutrition (HFS–215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–418–3098.

SUPPLEMENTARY INFORMATION: In a notice published in the **Federal Register** of March 7, 2000 (65 FR 12015), FDA announced that a food additive petition (FAP 0B4719) had been filed by Tritex Co., Inc., 1001 Boul. Industriel, Saint-Eustache (Quebec), CANADA J7R 6C3 (zip code was incorrectly identified as J7H 6C3 in the March notice). The petition proposed to amend the food additive regulations in § 176.170 *Components of paper and paperboard in contact with aqueous and fatty foods* (21 CFR 176.170) to provide for the safe use of sodium xylene sulfonated as a component of paper and paperboard intended to contact food. Although the additive was identified as sodium xylene sulfonated in the notice of filing, FDA feels that it is more appropriately listed as sodium xylenesulfonate in this final rule.

FDA has evaluated data in the petition and other relevant material. Based on this information, the agency concludes that the proposed use of the additive is safe, that the additive will achieve its intended technical effect, and therefore, that the regulations in § 176.170 should be amended as set forth below.

In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person listed above. As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

The agency has previously considered the potential environmental effects of this rule as announced in the notice of filing for FAP 0B4719. No new information or comments have been received that would affect the agency's previous determination that there is no significant impact on the human environment and that an environmental impact statement is not required.

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

Any person who will be adversely affected by this regulation may at any time file with the Dockets Management Branch (address above) written objections by June 26, 2000. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents are to be submitted and are to be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 176

Food additives, Food packaging.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, and redelegated to the Director, Center for Food Safety and Applied Nutrition, 21 CFR part 176 is amended as follows:

PART 176—INDIRECT FOOD ADDITIVES: PAPER AND PAPERBOARD COMPONENTS

1. The authority citation for 21 CFR part 176 continues to read as follows:

Authority: 21 U.S.C. 321, 342, 346, 348, 379e.

2. Section 176.170 is amended in the table in paragraph (b)(2) by alphabetically adding an entry under the headings ''List of substances'' and ''Limitations'' to read as follows:

§ 176.170 Components of paper and paperboard in contact with aqueous and fatty foods.

* * * * *

(b) * * *

(2) * * *

List of substances	Limitations
* * * * * * *	
Sodium xylenesulfonate (CAS Reg. No. 1300–72–7)	For use only in paper and paperboard coatings at levels not to exceed 0.01 percent by weight of the finished paper and paperboard.
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Dated: May 11, 2000.

L. Robert Lake,

Director of Regulations and Policy, Center for Food Safety and Applied Nutrition.

[FR Doc. 00–13209 Filed 5–25–00; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 200

[Docket No. 96N–0048]

RIN 0910–AA88

Sterility Requirement for Aqueous-Based Drug Products for Oral Inhalation

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations to require that all prescription and over-the-counter (OTC) aqueous-based drug products for oral inhalation be manufactured sterile. This rule applies to aqueous-based oral inhalation drug products in both single-dose and multiple-use primary packaging. Pressurized metered-dose inhalers are not subject to this rule. Based on reports of adverse drug experiences from contaminated nonsterile inhalation drug products and recalls of these products, FDA is taking this action to help ensure the safety and effectiveness of these products.

DATES: This rule is effective May 27, 2002.

FOR FURTHER INFORMATION CONTACT: Peter H. Cooney, Center for Drug Evaluation and Research (HFD–160), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–5818.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of September 23, 1997 (62 FR 49638), FDA proposed to amend its regulations to require that all inhalation solutions for nebulization be manufactured sterile. This action was proposed to help ensure the safety and effectiveness of these drug products.

Drug products for oral inhalation are used to treat a variety of breathing disorders and are frequently administered to patients who are immunocompromised, have cystic fibrosis, or have chronic obstructive airway disease. Aqueous-based oral inhalation drug products either in single-dose or multiple-use packaging are administered by oral inhalation into the lungs as a mist or spray created by a nebulizer device. The majority of inhalation drug products on the market are manufactured to be sterile. Those products not manufactured to be sterile are often manufactured under assigned microbial count limits, but current manufacturing methods and safeguards have not prevented dangerous microbial contamination.

Inhalation drug products contaminated with microorganisms are likely to cause lung infections because the contaminating organisms are introduced with the drug product directly into the lungs through the mouth. Thus, microbial contamination of these products may result in serious health consequences. Microbial contamination of these products may also cause degradation of the drug product.

Because of contamination problems with several different aqueous-based drug products for oral inhalation and for the reasons explained in the proposed rule, FDA has determined that current manufacturing methods and safeguards against contamination, including microbial limits tests, have not prevented dangerous microbial contamination of nonsterile aqueous-based drug products for oral inhalation.

The final rule reflects FDA's determination that all aqueous-based drug products for oral inhalation be manufactured sterile. Once the final rule becomes effective, failure to comply with the sterility requirement will result in a finding that the drug product is adulterated under section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 351(a)(2)(B)), and misbranded under section 502(j) of the act (21 U.S.C. 352(j)). Failure to comply with the sterility requirement will also result in the agency's refusal to approve a new or abbreviated application for a product, under section 505(d)(1), (d)(2), (d)(3), and (j)(4)(A) of the act (21 U.S.C. 355(d)(1), (d)(2), (d)(3), and (j)(4)(A)).

II. Highlights of the Final Rule

This final rule amends the regulations governing requirements for specific classes of drugs to include new § 200.51 for aqueous-based drug products for oral inhalation. Section 200.51(a) requires that all prescription and OTC aqueous-based drug products for oral inhalation be manufactured sterile. FDA is taking this action to prevent the public health consequences of the distribution of contaminated aqueous-based drug products for oral inhalation and to help ensure the safety and effectiveness of these products.

In the **Federal Register** of October 11, 1991 (56 FR 51354), FDA proposed to require that manufacturers use a terminal sterilization process when preparing a sterile drug unless the process adversely affects the drug product. The October 11, 1991, proposed rule would require that manufacturers include in their applications a written justification for not using terminal sterilization if such process is not appropriate. The agency plans to issue a final rule regarding terminal sterilization. When the proposed requirement for terminal sterilization becomes final, manufacturers of aqueous-based drug products for oral inhalation will be subject to its requirements.

The agency has revised the proposed regulation in response to comments received on the proposed rule. The comments and responses are discussed in section III of this document, ''Comments on the Proposed Rule.'' The agency is revising the title of proposed § 200.51 from ''Sterility Requirements for Inhalation Solution Drug Products'' to ''Aqueous-Based Drug Products for Oral Inhalation.'' The new title names the specific class of drugs subject to the rule in conformance with the established format of part 200 (21 CFR part 200), subpart C of the regulations. The agency is removing the phrases ''inhalation solution drug products'' and ''inhalation solutions for nebulization'' from proposed § 200.51. These phrases are replaced by the phrase ''aqueous-based drug products for oral inhalation.'' The agency has added the phrase ''for oral inhalation'' to clarify that the rule applies to orally administered inhalation drug products and not nasal sprays. The agency has added the modifier ''aqueous-based'' to the type of drug products covered to exclude metered-dose inhalers from coverage. In addition, the agency has made minor edits to the final rule in response to the President's June 1, 1998, memorandum on plain language in government writing. The agency has increased the amount of time for manufacturers to comply with the sterility requirement from 1 year to 2 years. All manufacturers of nonsterile aqueous-based drug products for oral inhalation will have until 2 years after the date of publication of the final rule to comply with the sterility requirement. As discussed in section IV of this document, ''Effective Date,'' the agency believes this effective date more realistically reflects the time